

## Evaluation of Clinical, Laboratory and Therapeutic Findings of Brucellosis among Children Hospitalized at Ardabil Hospitals

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**Abstract:** Goal and Precedents: Brucellosis is the common disease between human and animal and that is transmitted through contaminated animals. This study has been executed to determine clinical manifestation, laboratory findings and therapeutic approach of children afflicted by brucellosis, hospitalized at 2 hospitals (Aliasghar and Imam Khomaini) of Ardabil within 2000-2005. This study is a retrospective one, based on existing data of 51 medical units, belonging to patients that were hospitalized within 2000-2005 at these two centers diagnosed as brucellosis patients. From all 51 patients 76.5% were male. Familial history of brucellosis was positive among 38% of patients. Precedent of no pasteurized dairy consumption was seen among 62% of cases. Sixty nine percent of patients were belonging to high risk families. Clinical manifestations of disease were fever (84.2%) arthralgia (81.2%) perspiration (60.2%) lacking appetite (54%) Hepatomegaly (31%) splenomegaly (21%) and lymphadenopathy (18%). Laboratory findings were anemia (52.3%) leukopenia (41.2%) thrombocytopenia (4.5%) and leukocytosis (1.96%). Treatment in the majority of patients (76.2%) was Cotrimoxazole beside Rifampin or Gentamycin. The brucellosis was the cause of FUO in the 17.6% of cases. According to findings it seems that among children with fever and Arthralgia and especially with precedent of no pasteurized dairy consumption and being male this is essential to evaluate brucellosis possibilities. On the other hand it is advised to perform programs to inform members of high risk families about this disease.

**Key words:** Brucellosis, children, clinical and laboratory findings, therapeutic findings

### INTRODUCTION

Brucellosis is the common disease between human and animal that is transmitted through contaminated animals. This common infectious disease is created by gram negative aerobic coccobacil named as *Brucella*. *Brucella* contains various species. *B.Abortus*, *B. Melitensis*, *B.canis* and *B.swiss* are found in humans whereas other species found only in animals (Dennis *et al.*, 2005; Young *et al.*, 2000; Zvizdis *et al.*, 2006). This disease is animal infection that human is the incidental host and have no role in its reservation. The disease is transmitted through various ways and chiefly, non-pasteurized milk and cheese (Young, 2004). Prevalence of brucellosis at endemic regions varies from 0.01 to 200 in 100000 (Boschirali *et al.*, 2001). Persons who involve in dairy livestock and its byproduct like stockbreeders, farmers, veterinarians and butchers are more vulnerable to disease(Young, 2004). According to report of WHO Prevalence of brucellosis (human and animal) has been

increased in two recent decades at Mediterranean Sea domain, middle east countries, countries of west of Asia and some region of south America and Africa (Who, 1986; Corbel, 1997; Ratai, 2002). Iran and other 5 country of Eastern Mediterranean have had more than 90 thousands patients afflicted by brucellosis (Abdon, 1995). Continuation of traditional breeding methods and other factors like nutritional habits, personal and environmental hygienic issues and milk preparation method have made brucellosis as an endemic disease in our country (Jssa and Jmal, 1999).

Clinical manifestations range of brucellosis varies from a sub acute clinical to a chronic disease. Fever, perspiration, lacking appetite, suffocation, weight loss and depression are from manifestations. Arthritis is the most common form of local brucellosis that more involves hip and knee. Neurobrucellosis and Endocarditis are from hazardous but uncommon manifestations (Schutzie and Jacobs, 2004). Anemia, Leucopenia and Thrombocytopenia separately or in the

form of pancytopenia are seen in this disease (Young, 2004). One case of Thrombocytopenic purpura as single clinical manifestation of Brucellosis has been reported too (Yaloz *et al.*, 2000). Definite diagnosis is achieved by isolation of microbe from blood, bone marrow or tissues, however it should be noticed that culture of brucella needs prolonged incubation (Young, 2000; Dahouk *et al.*, 2003; Manture and Mangalgi, 2004; Joshi *et al.*, 2005).

Using BACTEC it has been possible to isolate this microbe from the articular fluid within one week (Yagupsky *et al.*, 2001). Serum agglutination tests with more than 1/160 titers support diagnosis and with 2ME we can say that disease is acute (Young, 2000; Yagupsky *et al.*, 2001; Irmak *et al.*, 2004). Brucellus treatment decrease signs, lessen complications and prevent relapse and chronic state. Therapeutic diets depend on age and underlying conditions. It has been advised to treat adults with Doxycyclin and Rifampin for 45 day or Doxycyclin for 45 day and Streptomycin for 20 day. A prescription of Tetracyclin for Childs under 8 year old and pregnant women is forbidden because of its effect on teeth. Then Cotrimoxazole beside Rifampin or Gentamycin is used. Relapse rate with these regimens is under 8% (Solera, 2000). In a study Mynocyclin that is one of the compositions of Tetracyclin was used and there was no side effect on teeth (Cascio *et al.*, 2004). Considering that familiarization with signs and symptoms of brucellosis has major role in controlling of disease and this issue has a big account in pediatrics, this study aim to determine common clinical manifestation and laboratory findings of brucellusis in pediatrics.

## MATERIALS AND METHODS

This is a retrospective study on the basis of existing data which in, medical units of 51 children, hospitalized with brucellosis diagnosis at Aliasghr and Imam Khomeini hospitals of Ardabil city from 2000 to 2005, were evaluated. The Diagnosis criteria are write test with more than 1/160 and clinical symptoms corresponding to disease. At first forms containing demographic information of patient, chief complaints, clinical and laboratory findings and treatment method were designed. Then forms were completed using hospital archive. Obtained data were analyzed with SPSS-11 software.

## RESULTS

From all 51 patients 39 case were male (76.5%) and their age average was 6.25 year (from 1.2 to 12 year old) Most of patients were referred at first half of year. 66% were living at village and rest were at city. 69% of patients

were belonging to high risk family with animal husbandry, farming, veterinary and butchery jobs. Positive familial history of brucellosis was seen in 38% and the rest patients (62%) had precedent of no pasteurized dairy. The most common findings were fever and arthralgia (84.2% and 81.2%). Knee and hip involvement and multi-articular involvement were seen in 39% and 44% of patients respectively. Anemia, leukopenia and leukocytosis were seen (52.3%, 4.5% and 1.96% respectively). ESR more than 50 was seen among 53% of patients and CRP was positive among 22%. The primary diagnosis on hospitalization was brucellosis only in 31.2% of patients and 9 case of patient have hospitalized with FUO diagnosis (17.6%). Wright test was positive in 47 cases (92%) and negative in the 4 cases. Coombs Wright requested for 31 cases, was positive in 96% and 2ME test that was requested for 19 cases, was positive in 78% of cases.

## DISCUSSION

In this study male female ratio was 3:1 which accords with finding of study executed by Manture on the high quantity of patients (Manture *et al.*, 2004). In the study of Shaalan *et al.* (2002) among 115 patients and study of Almuneef *et al* this ratio was 2:1 (Muneel *et al.*, 2003). In the study performed by Mamishi *et al* at the Tehran pediatric medical center, ratio was 2:1 too (Manishi *et al.*, 2006). More involvement of boys might caused by their more contact with animals.

Precedent of no pasteurized dairy consumption specially milk and cheese was positive among high number of patients that accords with results of Mature study at 2004. This is important because education of people to not consume not pasteurized dairy can be mandatory.

Concerning high contamination of no pasteurized dairy with brucellosis in our country this will be more important. Notwithstanding, it has been shown that using of hygienic belief pattern about transmission ways of brucellosis and harms of this disease for human and animals beside preventing behaviors training including using mask and gloves at work, washing of hands with water and soap and sunning of waste and evacuations, were been useful at high rate. On the other hand attention to this point in the medical history taking can help for diagnosis (Afsharian, 1999; Ghofrani, 1997; Fallan, 1995).

More than two third of patients was referred at spring and summer that can be induced by more dairy production and more fresh dairy consumption at these seasons and because of increased journeys at spring and summer to regions where fresh dairies are found in huge amount.

This seasonal outbreak can be used in considerable programming of country for preventing of disease.

The most common finding among clinical manifestations was fever (84.2%). Farzanegan (1991) reported fever as most common finding. Tsolia *et al.* (2002) in their study in the central parts of Greece about clinical, laboratory and therapeutic findings of their patients have noticed articular involvement as the most common finding. Mamishi *et al.* (2006) in their study on 44 patients have found articular involvement as most common finding (79.5%) and fever was at next rank (74.4%). Of course this issue have been the same in many studies. Young *et al.* (2000) also have mentioned this important issue in 5th edition of their Pediatric Infection book (Young, 2004). Hepatomegaly and splenomegaly were relatively common (31% and 21%) in our findings. This finding was the same in other studies. For example Hepatomegaly and splenomegaly had high prevalence (61% and 28%) in Tsolinâ€™s study. However Elbeltagy has mentioned these finding with lower prevalence, in his study (2001) on 137 children of Saudi Arabia (Elbeltagy, 2001). In our study Hepatomegaly had higher prevalence than splenomegaly, which is different from many of similar studies. In any way reticuloendothelial system is of beloved area for brucella for its proliferation and should be concerned in clinical studies.

This study has shown that brucellosis was cause of FUO in 17.6% of cases. In the study was done among 121 patients in India 4 case was afflicted by FUO (Handa *et al.*, 1998). In the study of Sen *et al.*, 6.8% of 414 patients with FUO were afflicted by Brucellosis. Likewise Kardi *et al.* (2000; 2002) have cited 0.8%. That confirms concerning of brucellosis in woke up and management of FUO, even in situation that manifestation of disease doesnâ€™t support brucellosis.

Number of WBC was normal or decreased in our patients. Anemia, thrombocytopenia and even pancytopenia were found in patients. There was a case of leucocytosis, too. ESR pattern wasnâ€™t constant (ESR>50 in 53%, ESR = 10-50 in 43% and ESR<10 in 3.95); altogether results of hematological tests as Young has said, arenâ€™t specific for diagnosis (Young, 2000; 2004). In brucellosis infection, all of uncomplicated patients that refer with acute symptoms, show good response to antibiotic therapy (Solera *et al.*, 1997; 2000). Our studied patients, have treated mainly with two regimens include Cotrimoxazole and Rifampin or Cotrimoxazole and Gentamycin and Tetracycline's compositions werenâ€™t used in child under than 8 year old. Relapse rate was high (4.2%) in these regimens. Cooperation of patients and their parents should be concerned for effectiveness of these regimens. In a study performed recently by Cascio *et al.* (2003) relapse rate of Mynocyclin and

Rifampin has reported lower than 2%. Miedang *et al.* (2003) have used 3 drugs for 6 week and wasnâ€™t seen any relapse. Manture that have used 3 drugs for 2 week and then 2 drugs for 6 week there were no relapse (Afsharian, 2004). Afsharian has shown in his study at Kermanshah that Cotrimoxazole and Rifampin have no relapse (Afsharian, 1999). Taheri SH has cited in his study that an 8 week simultaneous therapy by Doxycyclin and Rifampin was effective equal to Doxycyclin and Streptomycin. It has noted in this study that one of the factors, which reduce response to treatment (relapse or failure), is short period of pharmacotherapy (Taheri, 1995). Other compositions including Cotrimoxazole and Rifampin or Cotrimoxazole and Doxycyclin need more studies (Roushan *et al.*, 2004; Solera *et al.*, 2004; Miedang *et al.*, 2003; Bayindir *et al.*, 2003). Generally it seems that regarding brucella resistance versus present drugs, more study needs to be done.

## RECOMMENDATION

Concerning finding of this study it is recommended that through public training about not using of non-pasteurized dairies especially among residents of rural regions and other high risk groups effective strides in controlling of disease can be made. It seems also with seasonal outbreak of this disease, preventing programs should be focused at first half of year (spring and summer). Concerning that FUO cause was brucellosis in 17.6% of cases, it is recommended that staff of diagnosis and treatment direct more attention to this disease when encounter FUO. Finally it is suggested that more broad studies be done in the clinical levels for giving more successful treatments that have lower relapse and resistance.

## ACKNOWLEDGMENT

We should appreciate all archiveâ€™s staff of Imam Khomeini and Aliasghar hospitals and honorable authorities of these hospitals for their intimate cooperation. And we appreciate Mrs. Golmoghani ASL research expert of Ardabil university of medical science, that have encouraged us in finding of references.

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